

a median of 1.18/ μ L (range 0.20/ μ L–2.54/ μ L) and the ANC a median of 158/ μ L (range 0–1168/ μ L); 36/65 (55%) patients in DGD received no G-CSF (at physician's discretion) and those who received the drug did so starting on day 14 (median) post-transplant (range =11d–18d). There was no difference in the incidence or duration of \geq grade III mucositis, weight gain, rash or engraftment syndrome between DGD and CGD groups. However, as shown in Table 1 the CGD group had significantly faster engraftment, abbreviation of neutropenia, diminished antibiotics use, and shorter hospitalization. These effects were independent of CD 34 cell dose. Primarily because of abbreviated hospital stay, there was a 17% cost benefit to the use of CGD, supporting the overall benefit of this treatment regimen for patients with MM who receive ASCT.

Table 1

Characteristics	CGD group	DGD group	P value
Neutrophil Engraftment (days)	12 (11–14)	15 (11–20)	<0.0001
Duration of neutropenia (ANC <500)	7 (5–9)	10 (6–16)	<0.0001
Duration of severe neutropenia (ANC < 100) days	6 (4–9)	8 (4–10)	<0.0001
Duration of intravenous antibiotics	5 (3–20)	8 (3–15)	0.016
Duration of hospital stay	17 (14–24)	19 (16–28)	<0.0001

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Evaluation of Antioxidant Enzyme Levels of Glutathione Peroxidase in Patients Undergoing a Autologous Hematopoietic Stem Cell

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The Autologous Hematopoietic Stem Cell Transplantation (AHSCT) is a therapeutic method used in various immunological, hematological and genetic disorders, which uses patient's own stem cells collected from peripheral blood after their (the stem cells) mobilization by granulocyte colony-stimulating factors (G-CSF), in order to restore the damaged or defective bone marrow function. Oxidative stress and antioxidant depletion have been described during the stages involved in AHSCT. Glutathione peroxidase is an enzyme responsible for detoxification of organic and inorganic peroxides, which participates of enzymatic cellular antioxidant defense. The aim of the study was to evaluate the levels of glutathione peroxidase in various stages involving AHSCT in patients undergoing autologous hematopoietic stem cell transplantation. Glutathione peroxidase was determined using the Glutathione Peroxidase Ransel[®] kit (Randox). We measured glutathione peroxidase levels of eight patients at different times pre-and post-AHSCT: before Conditioning Regimen (CR), 24 hours after chemotherapy, 10 days (D +10) and 20 days (D +20) after transplantation. There was a statistically significant difference in levels of glutathione peroxidase after CR comparing to other times, suggesting an increase in oxidative stress after chemotherapy. According to previous studies, oxidative stress occurs acutely after high-dose chemotherapy for AHSCT and is apparently related to late hematological recovery. Thus, it can be suggested the use of glutathione peroxidase levels, and other

oxidative stress parameters as toxicity and grafting markers after AHSCT.

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A Multicenter Analysis of Intermediate-Dose Cyclophosphamide Versus Plerixafor and Granulocyte Colony Stimulating Factor for PB Progenitor Cell Mobilization in Patients with Multiple Myeloma Treated with Novel Induction Chemotherapies

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Introduction: Peripheral blood progenitor cell (PBPC) mobilization with intermediate-dose cyclophosphamide (3–4 gm/m²) (ID-CY) and G-CSF when compared to low-dose CY (1–2 gm/m²)-based strategies, has been shown to have a favorable risk/benefit profile in multiple myeloma (MM) patients (pts) receiving novel induction therapies. However the relative efficacy of ID-CY as compared to plerixafor (P) in PBPC mobilization in MM pts is not known. Herein we report outcomes of ID-CY/G-CSF mobilization compared to P/G-CSF mobilization in MM pts treated with novel induction regimens.

Methods: This multicenter outcomes study includes 84 pts who underwent a planned, single autograft within 1-year of starting induction therapy with novel chemotherapy agents (thalidomide, lenalidomide, bortezomib). Consecutive pts undergoing mobilization with ID-CY/G-CSF (3–4 gm/m²) (n=55) at one institution were compared against consecutive pts receiving plerixafor/G-CSF (0.24 mg/kg) (n=29) at a different transplant center. In order to assess efficiency of PBPC mobilization, we evaluated peak peripheral blood (PB) CD34+ cell counts, CD34+ cell yield on day1 of collection, total CD34+ cell collection, and total number of apheresis sessions. Mobilization failure was defined as failure to collect $\geq 2 \times 10^6$ cells/kg body weight. All pts with normal renal function received uniform conditioning with Mel200 (MEL140 if serum creatinine was ≥ 2 mg/dl).

Results: At baseline, the ID-CY and P cohorts were well balanced. No difference was observed in the use of lenalidomide (p=0.3). Compared to P, ID-CY use was associated with higher median peak PB CD34+ cell count (63/ μ L vs. 160/ μ L, P=.01), CD34+ yield on day 1 of collection (6.5 $\times 10^6$ /kg vs. 11.7 $\times 10^6$ /kg, P=.004), and total CD34+ cell yield (10.5 $\times 10^6$ /kg vs. 24.9 $\times 10^6$ /kg, P=.001). Median numbers of apheresis sessions were 2.2 in each group (p=0.9). No mobilization failures were seen in either group. There was no difference in the proportion of pts collecting $\geq 5 \times 10^6$ /kg CD34+ cells in either group (93% vs. 96%, P=.6), but more pts in ID-CY cohort collected $\geq 10 \times 10^6$ /kg CD34+ cells (55% vs. 78%, P=.02). Neutrophil engraftment was significantly faster (9.9

days vs. 13.1 days, $P < 0.001$) in the ID-CY pts, likely because of higher infused CD34+ cell dose. Rate of adverse events were higher in the ID-CY cohort including neutropenic fevers ($p=0.02$), intravenous antibiotic use ($p=0.03$), hospitalization ($p=0.05$) and packed red cell transfusions ($p=0.007$).

Conclusion: In the era of novel agents compared to P, ID-CY produced a more robust PBPC mobilization, faster engraftment, but was associated with significantly higher (but manageable) toxicity, and no difference in mobilization failure rates. These data support use of either intermediate dose - cyclophosphamide or plerixafor-based PBPC mobilization in MM pts undergoing stem cell collection following novel induction therapies.

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Hematopoietic Cell Yield Declines Predictably Over Time During Apheresis

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Hematopoietic cell (HC) mobilization to support high dose therapy is generally carried out using cytokines with or without chemotherapy. The resulting HC yield and the duration of cell collection have been well studied and tend to be variable. No consistent unifying relationship has been described which would reliably represent the kinetics of this process between different patients. To accomplish this, the HC yield from the mobilization procedures for 431 patients was examined. The diagnoses were multiple myeloma (N=220), non-Hodgkin's lymphoma (155) and Hodgkin's lymphoma (56). Mobilizing regimens included chemotherapy + G-CSF (97), G-CSF (232), G-CSF + plerixafor (84). To normalize the HC yield between patients, the total number of CD34+ cells collected on a given day was divided by the volume of blood (L) processed and was termed the HC mobilization index (HCMI). For the combined cohort the mean HCMI value on day 1 of apheresis (HCMI₁) was $19.7 (\pm 38.9) \times 10^6$ CD34+ cells/L/day. A significant correlation was found between HCMI₁ and the circulating CD34+ cell count on day 1 (R^2 0.69, $P < 0.01$), and the total HC yield in each patient (0.97 , $P < 0.01$). These observations were consistent in patients with various diagnoses and receiving different mobilizing regimens. Daily HCMI values were plotted over days of apheresis to determine the rate of change. A general trend of declining HCMI values over days of apheresis was observed, with some patients showing an initial increase. To offset the effect of the large range of HCMI values observed, the logarithm (log) of HCMI for each day was plotted against day of apheresis for each patient with >2 days of collection ($n=279$) to give individual log-HCMI decay curves. A quadratic equation ($y=ax^2+bx+c$) provided the best fit for these curves (mean R^2 0.88), demonstrating a parabolic relationship such that log HCMI increased and declined in proportion to square of time (in days) following the start of apheresis. It was noted that the values of coefficients were normally distributed in the study population; coefficient a (mean, -0.04 ± 0.2), b (0.04 ± 1.1), and c (1.7 ± 1.2). A Two-step cluster analysis of these coefficients distinguished three main groups (clusters) of patients. Patients in cluster 1 (38%) tended to have an initial increase in HCMI followed by an asymptotic decline; those in clusters 2 (50.2%) and 3 (8.6%) displayed declines of varying magnitude. Cluster 1 showed a higher proportion of NHL patients ($p=0.01$), whereas MM was over-represented in cluster 2 ($p=0.008$), consistent with

the notion that prior chemotherapy received by NHL patients impacted their mobilization kinetics. In conclusion, we demonstrate that HC yield during various mobilization procedures follows mathematically predictable kinetics which may reflect underlying hematopoietic reserve.

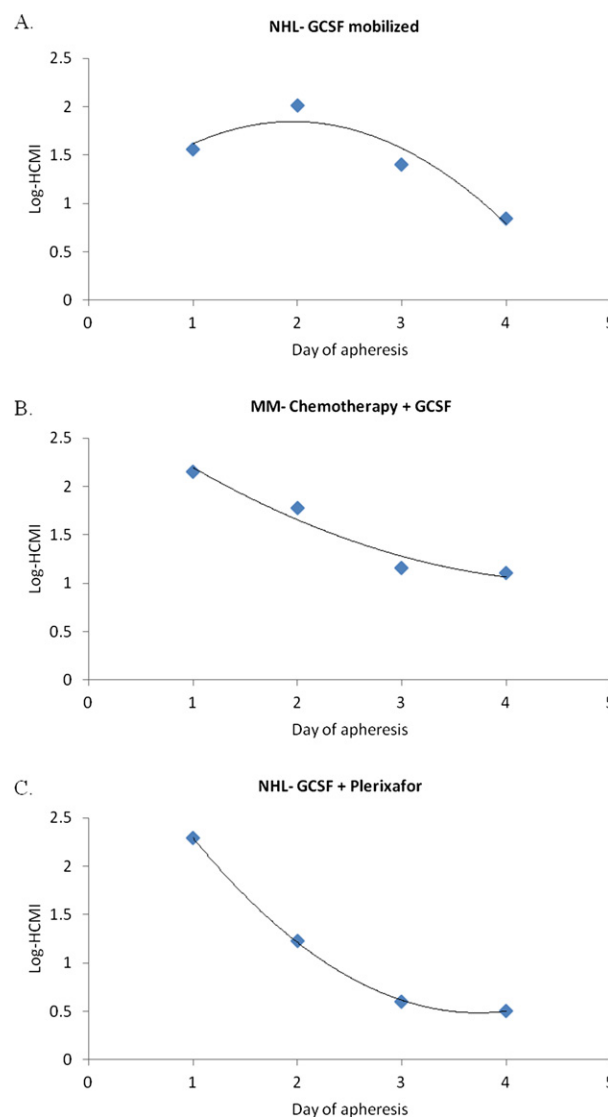


Figure 1. Log-HCMI decay curve: (A) Representative NHL patient from cluster 1; (B) Representative MM patient from cluster 2; (C) Representative NHL patient from cluster 3.

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Fluid Retention and Weight Gain During Peripheral Blood Hematopoietic Stem Cell Mobilization in Light Chain Amyloidosis

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Background: High-dose chemotherapy and autologous hematopoietic stem cell transplantation (auto-HCT) is an effective treatment for systemic light chain amyloidosis (AL). Fluid retention and weight gain during peripheral blood hematopoietic stem cell (PBSC) mobilization with growth